

## *n*-Butyl Pyridinium Nitrate as a Reusable Ionic Liquid Medium for Knoevenagel Condensation

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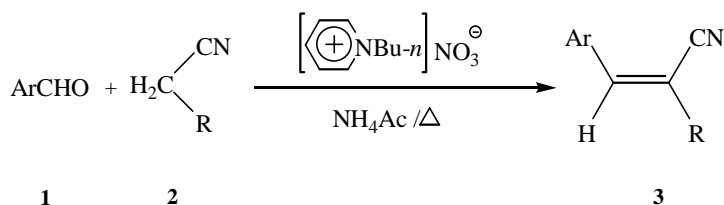
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**Abstract:** The Knoevenagel condensation of carbonyl substrates with active methylene compounds proceeds smoothly with ammonium acetate as catalyst in *n*-butyl pyridinium nitrate to afford the desired products of good purity in moderate yields.

**Keywords:** *n*-Butyl pyridinium nitrate, ionic liquid, Knoevenagel condensation.

Knoevenagel condensation is one of the most important preparation methods of substituted alkenes. It may be carried out either in homogenous or heterogeneous. The usual catalysts are organic bases<sup>1</sup> (primary, secondary and tertiary amines, ammonia and ammonium salts). Subsequently the uses of TiCl<sub>4</sub><sup>2</sup>, AlPO<sub>4</sub>-Al<sub>2</sub>O<sub>3</sub><sup>3</sup>, ZnCl<sub>2</sub><sup>4</sup>, KF<sup>5</sup>, LiCl<sup>6</sup>, K<sub>3</sub>PO<sub>4</sub><sup>7</sup>, TEBA<sup>8</sup> and CTMAB/H<sub>2</sub>O<sup>9</sup>, *etc.* have been reported. Recently, ionic liquids such as [hmim]PF<sub>6</sub><sup>10</sup> and BPyAlCl<sub>4</sub><sup>11</sup> as the green solvent have been proven to be an efficient method for Knoevenagel condensation. However these ionic liquids are not entirely satisfactory, due to such drawbacks as long reaction times and BPyAlCl<sub>4</sub> is unstable in moisture.

The use of ionic liquids as solvents has attracted much interest recently, partly due to their characteristic polar nature, phase behavior and lack of vapour pressure. In our continuous study of ionic liquids as recyclable media, we described here the Knoevenagel condensation for the synthesis of substituted alkenes based on the use of *n*-butyl pyridinium nitrate as a replacement for classic organic solvents (**Table 1**). The resulting alkenes can be easily separated from the ionic liquid system by extraction with an immiscible solvent diethyl ether. The ionic liquid is reused for the repeat run of the reaction with no diminution of the product yield.



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**Table 1** Knoevenagel reaction of aldehydes and active methylene compounds catalyzed by ammonium acetate in the *n*-butylpyridinium nitrate

Entry	Ar (1)	R (2)	Time(min)	m.p.(°C)	Lit.m.p. (°C)	Yields(%) <sup>a,b</sup>
a	4-MeO-C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> Et	30	79~81	79~81 <sup>7</sup>	77(81) <sup>c</sup>
b	4-OH-C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> Et	30	171~172	172.5~173 <sup>9</sup>	78
c	4-OH-3-MeO-C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	30	110~112	111~112 <sup>5</sup>	76
d	4-Me <sub>2</sub> N-C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> Et	30	124~125	124~126 <sup>5</sup>	83
e	C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> Et	30	51~52	50~51 <sup>7</sup>	72
f	4-Cl-C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> Et	30	92~94	92~94 <sup>7</sup>	75
g	4-MeO-C <sub>6</sub> H <sub>5</sub>	CN	15	115~116	115~116 <sup>7</sup>	80
h	4-Me <sub>2</sub> N-C <sub>6</sub> H <sub>5</sub>	CN	15	178~180	179~180 <sup>5</sup>	81
i	C <sub>6</sub> H <sub>5</sub>	CN	15	82~84	82~84 <sup>7</sup>	78
j	4-Cl-C <sub>6</sub> H <sub>5</sub>	CN	15	161~162	161~163 <sup>7</sup>	76

<sup>a</sup> Isolated yields<sup>b</sup> All of these compounds were confirmed by <sup>1</sup>H NMR and compared with authentic samples.<sup>c</sup> Yield in parenthesis obtained from the ionic liquid in the case of the fourth run

The <sup>1</sup>H NMR shows that only the E isomers of the olefinic products were produced. In conclusion, we have developed a simple and green procedure for the Knoevenagel condensation. The advantage of the present protocol is that the reaction is rapid, the yields are moderate, the procedure is simple and the solvent can be reused.

## Experimental

<sup>1</sup>H NMR spectra were recorded in CDCl<sub>3</sub> on a DRX-400 MHz instrument with TMS as an internal standard. *n*-Butyl pyridinium nitrate was prepared according to the literature<sup>12</sup>. Benzaldehyde was purified by distillation. All other chemicals used were of commercial grade without further purification.

### General procedure for the Knoevenagel condensations

A mixture of the aldehyde (5 mmol), active methylene compound (5 mmol) and NH<sub>4</sub>Ac (0.25 mmol) was stirred at 70°C in the *n*-butyl pyridinium nitrate (2 mL) for a given time (**Table 1**). The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was extracted with diethyl ether (5 mL×10). The organic extracts were then concentrated in vacuo. The resulting products were purified by recrystallization. Upon the completion of the washing, a second run using the ionic liquid was performed under the identical conditions without further manipulation.

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